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Original Article

Prognostic value of blood count parameters in patients with acute coronary syndrome

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ABSTRACT

Background: Recent studies have shown that complete blood count (CBC) parameters can effectively predict long-term mortality and re-infarction rates in acute coronary syndrome (ACS). However, the role of these parameters in predicting short term mortality has not been studied extensively. The main objective of this study was to determine whether CBC parameters can predict 30-days mortality and the incidence of major adverse cardiac event (MACE) in ACS patients.

Methodology: A total of 297 patients with ACS were recruited in this prospective study. The relationship of baseline white blood cell (WBC) to mean platelet volume ratio (WMR) with MACE and mortality was assessed during a 30-days follow-up. The patients were divided into two groups: Group A [WMR < 1000] and Group B [WMR > 1000]. Multivariate COX regression was performed to calculate hazard ratios (HR).

Results: WMR had the highest area under receiver operating characteristics curve and highest discriminative ability amongst all CBC parameters in predicting mortality. Patients in Group B had a higher mortality rate ($p < 0.001$) than patients in Group A. WBC count ($p = 0.02$), platelet count ($p = 0.04$), WMR ($p = 0.008$), platelet to lymphocyte ratio ($p < 0.001$) and neutrophil to lymphocyte ratio ($p = 0.03$) were significantly higher in the MACE-positive group as compared to MACE-negative. In Multivariate Cox regression analysis, WMR > 1000 (HR = 2.9, 95% confidence interval 1.3–6.5, $p = 0.01$) was found to be strongest biochemical marker in predicting mortality.

Conclusion: WMR is an easily accessible and an inexpensive indicator which may be used as a prognostic marker in patients with ACS.

1. Introduction

Although mortality rates of Acute Coronary Syndrome (ACS) have declined over the past four decades, it remains the leading cause of mortality and morbidity worldwide.[1] There is a 10% to 20% mortality rate in ACS patients within the first six months of diagnosis; with about half of all deaths occurring within the first 30 days.[2]

The pathophysiology of ACS is extremely heterogeneous; however in majority of the cases it is associated with rupture of an atherosclerotic plaque and partial or complete thrombosis of the infarct-related artery.[3] Ruptured plaques contribute to thrombus formation by inflammatory mechanisms, which include the role of activated and inactivated platelets and platelet-leukocyte adhesions, leading to the development of ACS.[4–6] Therefore, inflammatory biomarkers related to platelets and leukocytes can be used as prognostic tools and for risk stratification of ACS patients.

An elevated level of Mean Platelet Volume (MPV), a platelet activation marker, has been proven to be essential in detecting a cardiovascular event (CVE). The meta-analysis conducted by S.G. Chu et al. demonstrated that elevated MPV can be used to predict occurrence of acute myocardial infarction (MI), mortality following MI, and re-stenosis following coronary angioplasty.[7] Apart from MPV, other potentially useful complete blood count indices include leukocyte count, platelet count, Neutrophil to Lymphocyte Ratio (NLR), Platelet to Lymphocyte ratio (PLR), Red Cell

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Distribution Width (RDW) and white blood cell (WBC) to MPV Ratio (WMR).[8–10] Previous literature has mainly focused on the role of these biomarkers in predicting long term mortality and complications in ACS patients.

Recent studies have shown that the MPV and MPV/platelet count ratio can predict long-term mortality in patients with ischemic cardiovascular disease.[11,12] Similarly, in an analysis of 900 patients in the Stent Primary Angioplasty in Myocardial Infarction (Stent PAMI) trial, investigators found that an elevated WBC count upon hospital admission had a strong independent correlation with re-infarction and death at 1 year.[13] However, little is known about the suggested role of the aforementioned indicators, both individually and in combination, in predicting short term outcome in patients admitted for ACS.

Hence, in this prospective study, we sought to determine the efficacy of CBC parameters in estimating short-term mortality (30 days) and the incidence of Major Adverse Cardiac Events (MACE) in patients with ACS.

2. Materials and methods

This prospective cohort study was carried out at the Cardiology Department of the Civil Hospital, Karachi, Pakistan after approval from the Institutional Review Board (IRB) of Dow University of Health Sciences. From October 2015 to October 2016, all patients who presented with chief complaint of acute chest pain or were admitted at our institution with ACS were considered.

Adult patients diagnosed with ACS undergoing primary percutaneous intervention (PCI) were eligible for our study. ACS patients were identified by using the following criteria: non-ST elevation myocardial infarction (NSTEMI) was confirmed if patients had raised cardiac enzymes without detectable ST-segment elevation in the electrocardiogram (ECG). ST elevation myocardial infarction (STEMI) was confirmed if patient complained of typical chest pain lasting more than 20 min along with any one of the following characteristics: ST-segment elevation of at least 1 mm, formation of new Q wave, left bundle branch block formation in two or more contiguous leads, and/or two times increase in the cardiac enzymes. Unstable angina (UA) was confirmed if there were detectable ischemic changes on an ECG with no increase in cardiac enzymes.[8]

Patients were excluded if they were younger than 18 years, had received anticoagulant therapy or an immunosuppressant, had conditions which put them at high risk of serious bleeding, were diagnosed with cancer, active infectious diseases or inflammatory diseases, or severe liver disease.

A total of 350 patients were included in the study. Thirty-five patients refused to become part of the study, which narrowed the sample down to 315 patients. Seventeen patients were lost to follow-up which yielded a final sample size of 297.

On receiver operating characteristics (ROC) curve analysis, WMR had highest area under the curve (AUC) and highest discriminative ability amongst all CBC parameters in predicting mortality. Therefore, study population was divided into two groups according to their median values of WMR, namely: Group A [WMR $\leq$ 1000] and Group B [WMR $>$ 1000].

Once selected, an interviewer-based, pilot tested questionnaire was administered to each patient. Interviewer bias was eliminated by employing similarly qualified individuals, by training them and by keeping them unaware of the outcome of the study. Moreover, the questionnaire was translated into the national language, Urdu, for ease of understanding. Written and oral informed consent was obtained from all patients prior to administering the questionnaire.

At the time of inclusion, all patients were evaluated using a full physical examination and a detailed medical history. In addition, patients were further evaluated according to Killip clinical examination classification,[14] New York Heart Association (NYHA) classification[15] and Thrombolysis in myocardial infarction (TIMI) scores.[16]

One month following discharge, every patient was followed up by administering an interviewer-based, pilot tested questionnaire to record the incidence of major adverse cardiovascular events (MACE). MACE was considered positive if patients had any one of the following events: non-fatal MI, re-hospitalization, cardiac arrhythmias and death. In addition, other adverse events like cardiogenic shock, kidney dialysis, gastrointestinal (GI) bleeding, coronary artery bypass grafting (CABG) and access site complication were also recorded.

2.1. Laboratory analysis

At base line, venous blood samples were obtained within 30 min of admission to measure hematological indices and biochemical markers. An automated hematology analyzer SYSMEX XN-1000 was used to measure hematological indices. In addition, detailed liver function tests (LFTS), electrolytes, blood urea nitrogen (BUN) and creatinine (Cr) were measured with Roche Cobas c501 chemistry analyzer (Roche Diagnostics). Fasting lipid panels were measured by standard enzymatic methods. Patients were also evaluated for cardiac ischemia markers, echocardiography and a 12-lead ECG. Troponin I was measured by ChemiluminescenceMicroparticle Immune-Assay-CMIA (Cobas c601), while other cardiac enzymes were measured by Roche Cobas c 501. Left ventricular ejection fraction (LVEF) was assessed by two-dimensional echocardiography. Number of diseased vessel(s) (NODV) was evaluated after patients underwent coronary angiography.

2.2. Statistical analysis

Continuous variables were presented as mean $\pm$ standard deviation (SD) or as median (interquartile range), and analyzed for normality by the Shapiro-Wilk test. Categorical variables were compared using the Chi-square or Fisher's exact test while continuous variables were compared using Independent *t*-test or Mann-Whitney *U* tests. ROC curve analysis was conducted to determine prognostic accuracy of biochemical markers in predicting short-term mortality. Survival curve was generated by means of the Kaplan-Meier analysis. Those variables which had a $p < 0.25$ in univariate analysis were included in Multivariate COX regression analysis. The backward stepwise likelihood ratio method was used to identify the independent predictors of 30-days mortality. All tests were two-tailed and a p-value of less than 0.05 was considered significant. No imputation methods were used to replace missing variables. All analyses were performed with SPSS Statistics, version 17.0 (IBM SPSS Inc., Chicago, IL).

3. Results

The average age of the population was 55.4 $\pm$ 10.8 years while more than half (n = 188, 63.2%) of the patients were males. More than half (n = 210; 70%) of the patients were hypertensive, while 108 (36.4%) were known diabetics. Majority of the patients presented with either UA (n = 100, 33.7%) or with STEMI (n = 118, 39.7%). During the mean follow-up period of 29.5 days, 41 (13.8%) patients died due to cardiovascular events. Detailed comparisons of the baseline characteristics, clinical features, and biomarkers of the groups are shown in Table 1.

On comparison between Group A (WMR $<$ 1000, n = 160) and Group B [WMR $>$ 1000, n = 137], there was no significant difference in prevalence of co-morbid conditions such as diabetes (p = 0.312), hypertension (p = 0.63) and familial coronary artery disease (CAD)

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